SPECTROMAITRISE
CAPACITÉS

TRACEABILITY AND AUTHENTICATION OF PHARMACEUTICAL PRODUCTS

In the framework of increasingly stringent quality controls of health security, the pharmaceutical industry must deal with an increase of medicine counterfeiting. The latter becomes more and more sophisticated, and so more complicated to detect. According to the World Health Organization (WHO), a medicine is considered counterfeit when it is intentionally and fraudulently mislabeled with respect to its identity and/or its source. Taking counterfeit drugs may be inefficient when the active principle is missing or below the expected dose, or even dangerous when the medicines contain untested analogues.

Consequently, the different existing control organisms must verify in particular that raw materials and end products correspond to what is stated on the label. In order to guarantee the quality of medicines, these organisms are required to implement analytical tools to fight effectively against medicine counterfeiting. Nuclear Magnetic Resonance (NMR) is recognized as a powerful technique to answer this issue: indeed, it makes it possible to obtain the unique site-specific isotope profile of a molecule of interest (raw materials or finished products), and so to potentially discriminate between different synthesis processes and to verify that they correspond to those declared.

Which expertise is proposed by SPECTROMAITRISE?

- Characterization of raw materials and end products (medicines)
- Delivery of an internal marketing authorization

What are the innovative and differentiating methodologies used or proposed by SPECTROMAITRISE?

- Isotopic analyses at natural abundance on our spectrometers thanks to an expertise acquired for thirty years in this field
- Method transfer service to customers

To which matrices can the SPECTROMAITRISE expertise be applied?

- Raw materials for the manufacture of medicines
- Finished products (medicines)

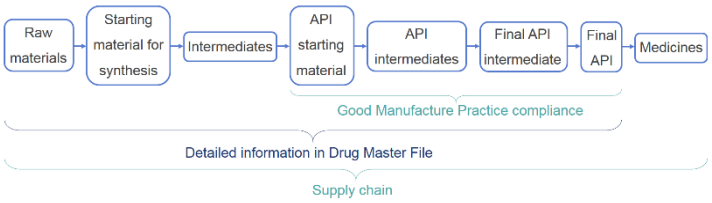
Examples of scientific and technical supports

SPECTROMAITRISE CAPACITÉS

NMR spectrometry isotopic fingerprinting: a tool for the manufacturer for tracking active pharmaceutical ingredients from starting materials to final medicines,

G. Remaud *et al.*, *European Journal of Pharmaceutical Sciences*, 2013, 48, 464-473

This publication shows the relevance of using NMR to access site-specific isotope contents at natural abundance. The latter were measured on active pharmaceutical ingredients by ^{2}H and ^{13}C NMR in order to provide complementary information that could help to characterize the manufacturing process. The analyses of twenty commercial ibuprofen samples led to a unique intramolecular isotope identification as well as a preliminary classification of these samples according to the synthetic process behind their manufacturing.

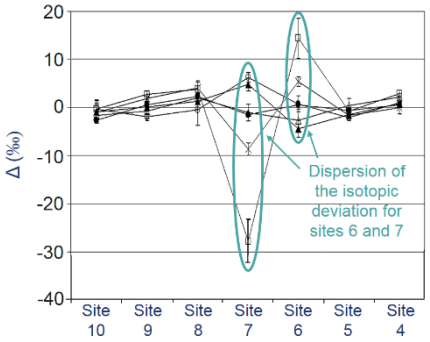


Traceability workflow for active pharmaceutical ingredients

Isotopic finger-printing of active pharmaceutical ingredients by ^{13}C NMR and polarization transfer techniques as a tool to fight against counterfeiting,

U. Bussy *et al.*, *Talanta*, 2011, 85, 1909-1914

In this article, the acquisition parameters of INEPT sequence are optimized in order to be able to analyze several ibuprofen samples in a short time without deterioration of the accuracy of isotopic measurements. The results obtained on samples from different origins allowed to compare the isotopic ^{13}C distribution within a given molecule: this methodology is proposed as a suitable tool to fight against counterfeiting.



Isotopic deviations obtained for ibuprofen samples from different origins

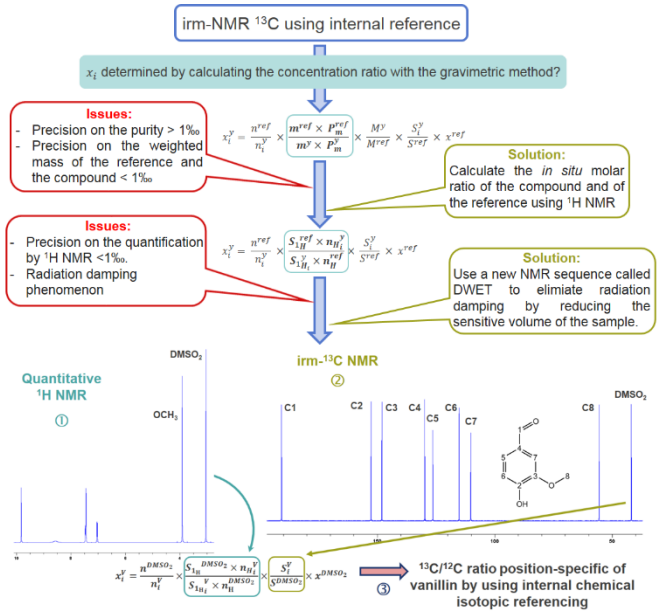
Isotopic ^{13}C NMR spectrometry to assess counterfeiting of active pharmaceutical ingredients: site-specific ^{13}C content of aspirin and paracetamol,

V. Silvestre *et al.*, *Journal of Pharmaceutical and Biomedical Analysis*, 2009, 50, 336-341

This publication demonstrates that quantitative isotopic ^{13}C NMR is a promising tool for the fight against counterfeiting of medicines. The analyses were carried out on paracetamol and aspirin samples from different countries: they allowed the establishment of site-specific isotopic profiling of these active pharmaceutical substances and their discrimination according to their origin.

The new face of isotopic NMR at natural abundance,

T. Jézéquel *et al.*, *Magnetic Resonance in Chemistry*, 2017, 55, 77-90



This article sums up the major improvements made for thirty years in the field of isotopic analyses by NMR. After reminding some important definitions, different applications by ^{2}H and ^{13}C NMR are presented in which technical improvements were made to reach the required accuracy of a few ‰ for instance, or to suppress undesired phenomena such as radiation damping.

Schematic illustrating how to obtain ^{13}C position-specific ratios with a high precision quantitative NMR strategy